## REMARKS

### I. Claim Status

After entry of this amendment, claims 11-19 will be pending. The Office has withdrawn claims 14-16 from consideration as being directed to a non-elected invention. Dec. 11, 2009, Final Office Action at 2. Applicants have added new claims 17-19, which recite the chemical compounds recited in pharmaceutical composition claims 11-13, respectively. No claims have been amended herein.

Applicants respectfully acknowledge that the Office has withdrawn the rejection of claims 11-13 under 35 U.S.C. § 103(a) over Blaakmeer in view of Patani et al., "Bioisosterism: A Rational Approach in Drug Design," Chem. Rev., 96:3147-76 (1996). Mar. 16, 2011, Final Office Action at 2.

### II. Interview Summary

Applicants thank the Examiner for his time on August 10, 2011, to discuss this application with Applicants' undersigned representative. During the August 10, 2011, interview, the undersigned and the Examiner discussed adding new claims 17-19 reciting the chemical compounds recited in pharmaceutical composition claims 11-13, respectively, i.e., the chemical compounds in claims 17-19 are commensurate in scope with the chemical compounds recited in pharmaceutical composition claims 11-13. The Office restricted the claims as originally filed in a February 4, 2009, Office Action. Applicants elected claims directed to pharmaceutical compositions and cancelled the claims directed to the compounds in the pharmaceutical compositions. *See* Apr. 3, 2009, Response to Office Action. The Examiner indicated that he would consider

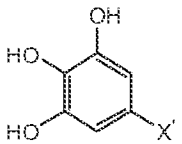
rejoining such compound claims once the pharmaceutical composition claims are found allowable.

## III. Double Patenting Rejection

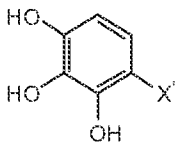
The Office maintains the rejection of claims 11-13 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 12/067,059 ("the '059 application").[1] *See* Mar. 16, 2011, Final Office Action at 2-4. The Office states that the conflicting claims are not patentably distinct because the compounds of the present application and copending '059 application are "positional isomers." *Id.* at 3.

Applicants respectfully traverse for the following reasons.

The present application claims a pharmaceutical composition comprising at least one compound of formula (C) or (D):

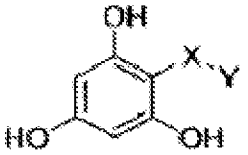



C




D

In contrast, claim 1 of the '059 application recites a compound of formula (I):




I

Applicants note that the claimed compounds have unexpected, beneficial properties that compounds falling within claims 1-6 of the '059 application do not have.

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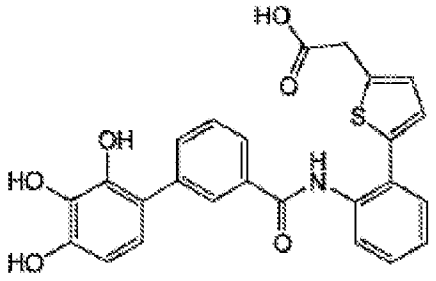
[1] The '059 application recently issued as U.S. Patent No. 7,919,532.

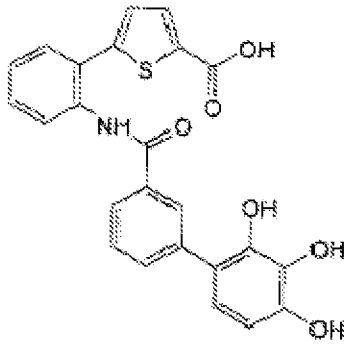
Indeed, one of skill in the art would not have reasonably expected that the 2,3,4- and 3,4,5-hydroxy substitution pattern on the phenyl ring of the claimed compounds would have resulted in such properties as compared with the 2,4,6-hydroxy substitution pattern of the '059 application. Specifically, Applicants tested compounds falling within the scope of the present application and claims 1-6 of the '059 application and compared their inhibition of either E- or P-selectin. *See* Declaration of Dr. Remo Kranich Under 37 C.F.R. § 1.132 ("Kranich Declaration"), attached herewith.

The testing results demonstrate that the claimed compounds are more stable than structurally similar compounds tested in the '059 application. The following compound, corresponding to compound 48 of the present application, was prepared according to the methods in the present application:

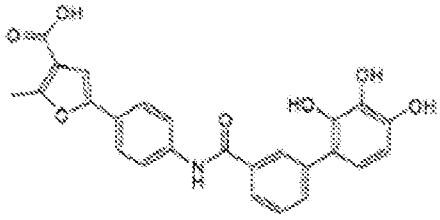



(48)

*See* Kranich Declaration at 2. The following two compounds were also prepared according to the present application and fall under the scope of the claims of the present application:



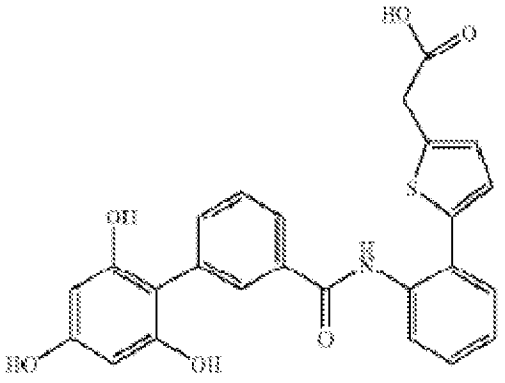
(A)



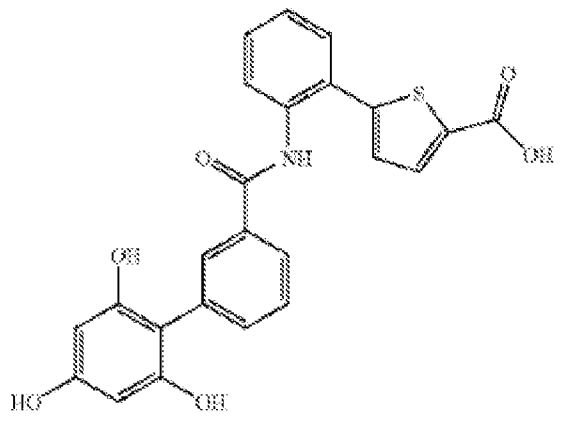
(B)

*See id.*

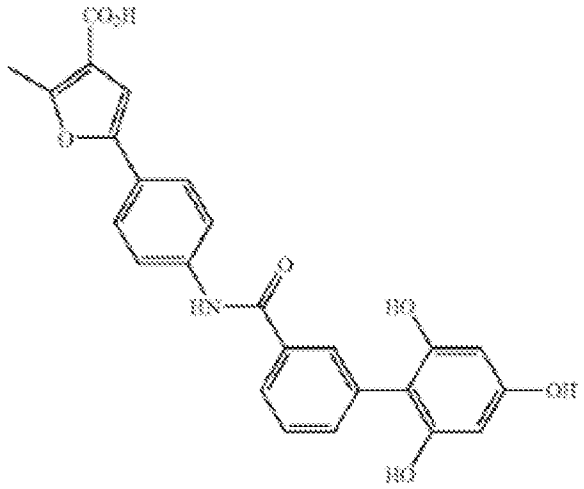
The following compounds corresponding to Compounds 63, 26, and 60 of the '059 application, which are structurally identical to compounds 48, (A), and (B) above, except for the respective hydroxy group substitution pattern on the phenyl ring, were prepared according to the methods described in the '059 application:



(63)



(26)



(60)

*See* Kranich Declaration at 2.

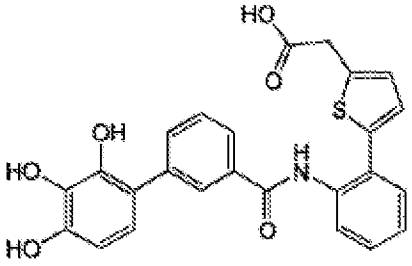
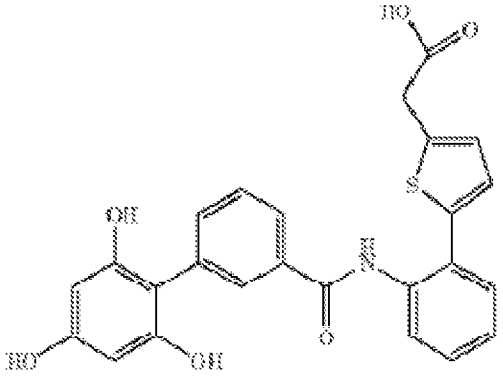
As the following Table 1 shows, the 2,3,4- and 3,4,5-hydroxy substituted phenyl compounds of the present invention (e.g., 48, (A), and (B)) have a higher normalized inhibition of either E- or P-selectin than the 2,4,6-hydroxy substituted phenyl compounds according to the '059 application (e.g., 63, 26, and 60). *See* Kranich Declaration at 3, 5. Specifically, Table 1 compares the experimental data concerning the inhibition of cell binding, which is described in the Flow Chamber Assay disclosed in the present application on page 33 of U.S. Patent Application Publication No. 2008/0249107 and page 44 of the '059 application (*see* U.S. Patent Application Publication No. 2008/0207741 at page 23-24, ¶¶ [0185]-[0187]). *See* Kranich Declaration at 3. The

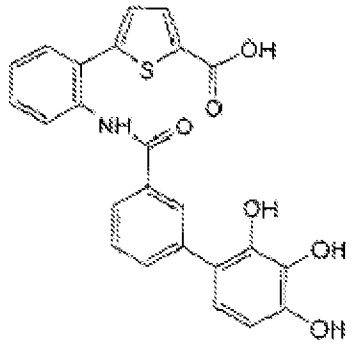
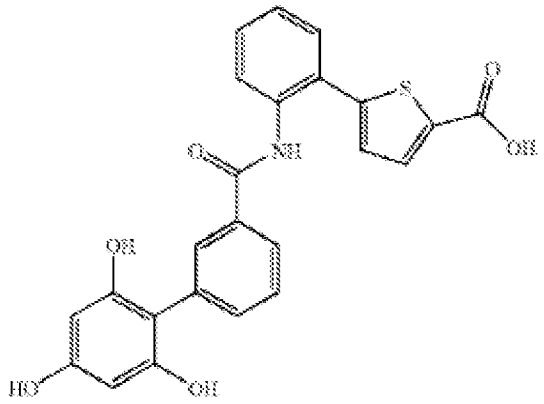
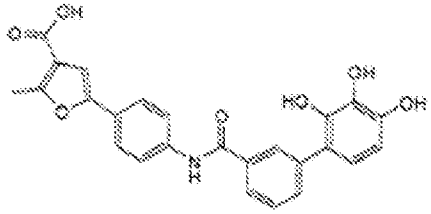
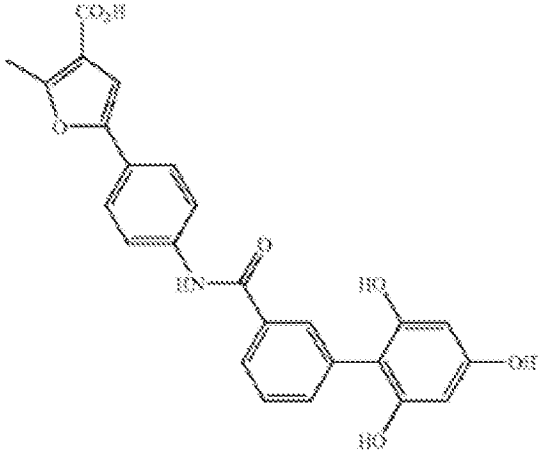
value of the inhibition ratios are given as normalized ratio of %-inhibition of the respective compound divided by %-inhibition of the selectin inhibition standard compound Bimosiamose (1,6-Bis[3-(3-carboxymethylphenyl)-4-(2-α-D-mannopyranosyloxy)-phenyl]hexane):

[inhibition ratio] = [%-inhibition of compound] / [%-inhibition of standard (Bimosiamose)]

*See* Kranich Declaration at 3.

Table 1:

| **Chemical Structure** | **Inhibition Ratio of i) E-selectin ii) P-selectin** | **Chemical Structure** | **Inhibition Ratio of i) E-selectin ii) P-selectin** |
|---|---|---|---|
| Compound Example 48 from pending U.S. Pat. App. No. 10/593,259  | i) 1.4<br>ii) 2.0 | Compound Example 63 from U.S. Pat. App. No. 12/067,059  | i) 1.2<br>ii) 0.9 |

| **Chemical Structure** | **Inhibition Ratio of i) E-selectin ii) P-selectin** | **Chemical Structure** | **Inhibition Ratio of i) E-selectin ii) P-selectin** |
|---|---|---|---|
| Compound (A) according to pending U.S. Pat. App. No. 10/593,259  | i) 2.0<br>ii) 2.6 | Compound Example 26 from U.S. Pat. App. No. 12/067,059  | i) 1.1<br>ii) 0.8 |
| Compound (B) according to pending U.S. Pat. App. No. 10/593,259  | i) 1.4<br>ii) 1.5 | Compound Example 60 from U.S. Pat. App. No. 12/067,059  | i) 1.0<br>ii) 1.0 |

*See* Kranich Declaration at 4.

The Flow Chamber Assay procedure used was identical to the procedure described in the present application (*see* U.S. Pat. App. Pub. No. 2008/0249107 at ¶¶ [0164]-[0165]) and the'059 application (*see* U.S. Pat. App. Pub. No. 2008/0207741 at ¶¶ [0185]-[0187]). *See* Kranich Declaration at 2-3.

One of skill in the art would not have reasonably expected that compounds covered by the pending claims in the present application would have a higher normalized inhibition of either E- or P-selectin than compounds covered by the claims in the '059 application.

Accordingly, Applicants respectfully submit that claims 1-6 of the '059 application do not render the claimed invention obvious, and the double patenting rejection should be withdrawn.

## Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

If the Examiner believes a telephone conference could be useful in resolving any outstanding issues, the Examiner is respectfully invited to contact Applicants' undersigned counsel at (703) 776-9703.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 50-5410.

Respectfully submitted,

J.A. LINDEMAN & CO. PLLC

Date: August 15, 2011

By: /Aaron M. Raphael, Reg. No. 47,885/
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**Attachment:** Declaration of Dr. Remo Kranich Under 37 C.F.R. § 1.132